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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/757,212	01/09/01	SEDRANI	R 100-8024C/C1

001095
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EXAMINER	
CEPERLEY, M	
ART UNIT	**PAPER NUMBER**
1641	6

DATE MAILED: 10/03/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/757,212	Applicant(s) SEDRANI ET AL.	
	Examiner Mary E. (Molly) Ceperley	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *1-7 and 11-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2 .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

1. Applicants' election of Group II, claims 8-10 in Paper No. 4 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 8-10 are rejected under 35 USC 103(a) as being obvious over each of references ***(1)***: Stella et al (U.S. 4,650,803), Failli et al (A) (U.S. 5,177,203), Kao et al (U.S. 5,118,678), Kao (U.S. 5,194,447), Caufield (U.S. 5,118,677), Amer. Home Prods. (WO 92/05179), or Failli et al (B) (U.S. 5,130,307) taken in combination with each of references ***(2)***: Sevier et al (Clinical Chemistry, 27/11, 1797-1806 (1981)), Yelton et al (American Scientist, 68, 510-516 (1980)), or Campbell et al (Monoclonal Antibody and Immunosensor Technology, Chapter 1, Elsevier (1991)) and each of references ***(3)***: Rosenthaler et al (U.S. 5,169,773) or Erlanger (Methods in Enzymology, Vol. 70, 85-104 (1980)).

Each of references ***(1)*** describes pharmaceutically active rapamycin derivatives which are substituted at the positions which correspond to either the 40- or 28-position of the rapamycin compounds as depicted in structure (III) of page 4 and Formula B of page 8 of the instant application. Please note that the 40-position of the rapamycin ring

may be equivalently described as the 42- position and that the 28- position may be described as the 31- position depending on the numbering system used by a given set of authors/inventors. See Stella et al: Figure 1; col. 1, lines 49-68; Failli et al (A): structure (I); Kao et al: col. 1, line 45 – col. 2, line 34; Kao: abstract; Caufield: abstract; Amer. Home Prods.: title and abstract; Failli et al (B): abstract. These references establish that rapamycin 40- or 28-substituted rapamycin derivatives are well known pharmaceutically active agents. These references do not describe the production of antibodies specific for these pharmaceutical agents.

References ***(2)*** establish that it is well known in the art that monoclonal antibodies to an extremely wide variety of known antigens may be prepared using conventional immunogenic hapten-carrier conjugates. See Sevier et al, the entire article, in particular, Table 2; Yelton et al: the entire article; Campbell: the entire article, in particular, section 1.17.6.

References ***(3)*** describe conventional techniques for preparing immunogenic protein-hapten conjugates in which the hapten contains an active hydroxy functional group as does rapamycin. See Rosenthaler et al: Examples 3, 4 and 7 in which an immunogenic conjugate is formed using an succinimidooxysuccinyl derivative (analogous to the hapten derivative of instant claim 10) of a macrocyclic compound; Erlanger: page 97, *Hemisuccinates*.

Given the fact that 40- and 28- substituted rapamycin derivatives are well known drugs (references ***(1)***) and that antibodies produced specific to well known drugs have an expected utility (references ***(2)***), it is considered to be well within the level of skill in

the art and therefore obvious to substitute rapamycin derivatives as haptens in a conventional method of preparing immunogenic conjugates (references ***(3)***) with the expectation of obtaining the corresponding claimed rapamycin immunogens which would be useful in the preparation of antibodies specific for rapamycin and its derivatives. See *Ex parte Erlich,* 3 USPQ2d 1011, in particular, page 1015, column 1.

4. Claims 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over each of references ***(1)***, ***(2)***, and ***(3)*** of paragraph 3. above and further in combination with Niwa et al (U.S. 5,532,137).

References ***(1)***, ***(2)***, and ***(3)*** are applied for the reason stated in paragraph 3. above.

Niwa et al is applied for its description of the preparation of immunogens which use FR-900506, a macrocyclic structure very similar to rapamycin, as a hapten. See the structure of col. 7 where the point of attachment of the linker is at a position which corresponds to the 40-position of the instant rapamycin derivative and the monoclonal antibody production of Example 2.

Given the fact that 40- and 28- substituted rapamycin derivatives are well known drugs (references ***(1)***), it is considered to be well within the level of skill in the art and therefore obvious to substitute these derivatives as haptens in conventional methods of preparing immunogenic conjugates as described in references ***(2)*** and ***(3)*** with the

expectation of obtaining the claimed immunogens which would be useful in the preparation of antibodies specific for the 40- and 28-substituted rapamycin epitopes. This is particularly true in view of the further teaching of Niwa et al that antibodies to very structurally similar macrocyclic compounds can be prepared using 40-substituted hapten/carrier conjugates.

5. Morrison et al (U.S. 5,750,413: Figure 1, reaction scheme (iii) and col. 9, lines 21-32) and Legay et al (U.S. 6,187,547: col. 5, lines 7-35) are cited to further show the state of the art.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. (Molly) Ceperley whose telephone number is (703) 308-4239. The examiner can normally be reached from 8 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-7230.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

September 27, 2001

Mary E. Ceperley

MARY E. CEPERLEY
PRIMARY EXAMINER
ART UNIT ~~122~~ 1641

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